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Role of Tissue Inhibitor of Metalloproteases-1 in Junction Dynamics in the Testis

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Using multiple high-performance liquid chromatography steps, we have identified and purified a polypeptide to apparent homogeneity from primary Sertoli cell conditioned culture medium that consisted of 2 molecular variants of 31 and 29 kDa when electrophoresed on a sodium dodecyl sulfate–polyacrylamide gel run under reducing conditions. Partial N-terminal amino acid sequence analysis of these 2 proteins revealed a sequence of NH_2-IKMAKMLKGFDAVGNATG, which is homologous to tissue inhibitor of metalloproteases-1 (TIMP-1). Studies by semiquantitative reverse transcription-polymerase chain reaction using a primer pair specific to rat TIMP-1 demonstrated that both Sertoli and germ cells express TIMP-1. During maturation, the steady-state TIMP-1 mRNA level in the testis increased significantly from 40 to 60 days of age, which suggests its role in the restructuring of the epithelium during spermiation. This increase in testicular TIMP-1 expression was apparently not due to the increase in germ cell number, because TIMP-1 expression decreased approximately fivefold in germ cells isolated from testes of aging rats. Using Sertoli cells cultured at low (0.05×10^6 cells/cm^2) and high (0.5×10^6 cells/cm^2) densities, it was found that TIMP-1 expression increased transiently but significantly during junction assembly. A similar induction of TIMP-1 mRNA was also detected in Sertoli–germ cell cocultures during germ cell adhesion onto Sertoli cells. More important, the inclusion of either α_2-macroglobulin (a protease inhibitor produced by Sertoli cells) or aprotinin (a serine protease inhibitor) into an in vitro germ cell adhesion assay facilitated the attachment of fluorescently labeled germ cells onto the Sertoli cell epithelium when compared to control, which suggests that the assembly of adherens junctions may involve protease inhibitors.

Key words: Protease inhibitor, Sertoli cell, germ cell, tight junction, adherens junction

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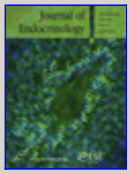
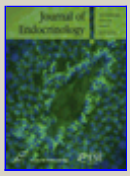
D. D. Mruk, A. S. N. Lau, O. Sarkar, and W. Xia
Rab4A GTPase Catenin Interactions Are Involved in Cell Junction Dynamics in the Testis
J Androl, September 1, 2007; 28(5): 742 - 754.
[Abstract] [Full Text] [PDF]



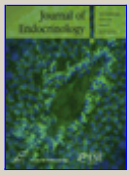
Journal of Endocrinology HOME

W. Xia, D. D Mruk, W. M Lee, and C Y. Cheng
Unraveling the molecular targets pertinent to junction restructuring events during spermatogenesis using the Adjudin-induced germ cell depletion model
J. Endocrinol., March 1, 2007; 192(3): 563 - 583.
[Abstract] [Full Text] [PDF]



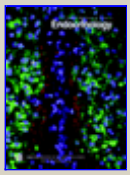
Journal of Endocrinology HOME

N. P Y Lee, D. D Mruk, W. Xia, and C Y. Cheng
Cellular localization of sphingomyelin synthase 2 in the seminiferous epithelium of adult rat testes
J. Endocrinol., January 1, 2007; 192(1): 17 - 32.
[Abstract] [Full Text] [PDF]



Journal of Endocrinology HOME

P. P Y Lie, W. Xia, C. Q F Wang, D. D Mruk, H. H N Yan, C.-h. Wong, W. M Lee, and C Y. Cheng
Dynamin II interacts with the cadherin- and occludin-based protein complexes at the blood-testis barrier in adult rat testes
J. Endocrinol., December 1, 2006; 191(3): 571 - 586.
[Abstract] [Full Text] [PDF]



Endocrinology HOME

C.-h. Wong, D. D. Mruk, M. K. Y. Siu, and C. Y. Cheng
Blood-Testis Barrier Dynamics Are Regulated by {alpha}2-Macroglobulin via the c-Jun N-Terminal Protein Kinase Pathway
Endocrinology, April 1, 2005; 146(4): 1893 - 1908.
[Abstract] [Full Text] [PDF]

ENDOCRINE REVIEWS HOME

D. D. Mruk and C. Y. Cheng
Sertoli-Sertoli and Sertoli-Germ Cell Interactions and Their Significance in Germ Cell Movement in the Seminiferous Epithelium during Spermatogenesis
Endocr. Rev., October 1, 2004; 25(5): 747 - 806.
[Abstract] [Full Text] [PDF]

BIOLOGY of REPRODUCTION HOME

M. K.Y. Siu and C. Y. Cheng
Extracellular Matrix: Recent Advances on Its Role in Junction Dynamics in the Seminiferous Epithelium During Spermatogenesis
Biol Reprod, August 1, 2004; 71(2): 375 - 391.
[Abstract] [Full Text] [PDF]

HUMAN REPRODUCTION UPDATE HOME

N. P.Y. Lee and C. Y. Cheng
Ectoplasmic specialization, a testis-specific cell-cell actin-based adherens junction type: is this a potential target for male contraceptive development?
Hum. Reprod. Update, July 1, 2004; 10(4): 349 - 369.
[Abstract] [Full Text] [PDF]

BIOLOGY *of* REPRODUCTION HOME

M. K.Y. Siu and C. Y. Cheng
Interactions of Proteases, Protease Inhibitors, and the {beta}1 Integrin/Laminin {gamma}3 Protein Complex in the Regulation of Ectoplasmic Specialization Dynamics in the Rat Testis
Biol Reprod, April 1, 2004; 70(4): 945 - 964.
[Abstract] [Full Text] [PDF]

Journal of Cell Science HOME

C.-h. Wong, D. D. Mruk, W.-y. Lui, and C. Y. Cheng
Regulation of blood-testis barrier dynamics: an in vivo study
J. Cell Sci., February 15, 2004; 117(5): 783 - 798.
[Abstract] [Full Text] [PDF]